Rapid Myocardial Calcification
After Cardiac Surgery

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SINCE the advent of cardiac surgery, considerable work has appeared on acid-base and electrolyte balance in the postoperative period, but relatively little of it has concerned calcium. We recently observed a case of rapid myocardial calcification after cardiac surgery and present it as an unusual addition to the existing literature on abnormal myocardial calcification.

Report of a Case

An eight-year-old boy entered the hospital in June, 1962, for investigation of a cardiac murmur. Two years previously cardiac surgeons at another institution had repaired uneventfully a coarctation of the aorta and a patent ductus arteriosus. The boy's physician, however, discovered a new murmur shortly before the current admission. Past medical history, family history, and review of systems were not contributory. Physical examination showed a well-developed but slender, 50 lb (22.8 kg), child in no distress. The blood pressure was 85/58 mm Hg in the right arm and 98/60 mm Hg in the left arm. The pulse was 90 beats per minute, and the peripheral pulses were equal and of good quality. The heart was enlarged to percussion, and a grade four systolic ejection murmur with thrill was loudest along the third interspace of the left sternal border. The chest showed a well-healed thoracotomy scar, and the lungs were clear and resonant. The hemoglobin, hematocrit, white blood cell count, sedimentation rate, prothrombin activity, blood glucose, blood urea nitrogen, and urinalysis all were within normal limits. Electrocardiograms showed left ventricular hypertrophy and ischemia of the posterior left ventricle. Chest roentgenograms showed an enlarged heart with increased hilar markings in otherwise clear lung fields, plus an inappreciable aortic arch. Cardiac catheterization studies suggested obstruction of the left ventricular outlet near the aortic valve. Accordingly, on June 21, under general (halothane [Fluothane]-oxygen) endotracheal anesthesia, partial cardiac bypass, and 30° C hypothermia, the patient underwent left ventriculotomy and excision of an infundibular aortic stenosis directed by direct vision. A mitral valve stenosis and a large aneurysm of the sinus of Valsalva were also corrected through a transaortic approach. The heart was markedly enlarged at operation but disclosed no gross calcific changes; histochemical examination (hematoxylin and eosin, Alizarin Red S, Von Kossa's stain) of the right and left atria and of the left ventricle's stenotic area biopsied at the operation confirmed the absence of abnormal calcium deposits (Fig 1). It was difficult to sustain the blood pressure and to obtain satisfactory perfusion pressure during the 5½ hour procedure. Near the end of the procedure the child received intravenously 5.4 mEq of calcium as calcium chloride. Promptly regaining consciousness, he remained alert and cooperative during the first 8 postoperative hours, but thereafter lapsed into deepening stupor and coma. Electrocardiograms 1 day after surgery showed complete A-V block and a marked change in polarity since the preoperative tracing. On the second day an external cardiac pacemaker terminated two episodes of asystole, although subsequent electrocardiograms did not change from those of the previous day. Urinary output totalled 455 ml during the 6-day postoperative period. Despite mannitol infusions, the BUN climbed to 74 mg/100 cc. Because of increasing signs of cardiac failure, a serum potassium of 6.3 mEq/liter, and a total serum calcium of 2.9 mEq/liter, calcium totaling 51.4 mEq as gluconate and chloride was infused intravenously beginning 12 hours postoperatively and continuing intermittently for 4 days. Six subsequent total serum calcium levels remained between 3.2 and 4.8 mEq/liter. A single serum inorganic phosphate level on the fourth postoperative day was 5.6 mEq/liter. Multiple determinations of serum
sodium, chloride, and arterial pH were within normal limits. Serum magnesium and urinary calcium studies were not done. The patient received between 50 and 100 mEq of aerosol isoproterenol and 1,600 mg of parenteral hydrocortisone, but no vitamin D or congeneres during this period. His dietary intake of calcium was zero. Despite every effort, signs of cerebral edema and cardiac failure gradually increased and the patient died during a period of refractory bradycardia on the sixth postoperative day.

At autopsy the body showed no signs of bony change or deformity. The markedly enlarged heart weighed 250 gm (normal for age: 138 gm). It showed, in addition to the expected evidence of congenital deformity and operative intervention, a striking yellow granular streaking of the right and left atrial and ventricular myocardium which, although it involved the operative and biopsy sites, was not confined to them. Histological examination of these gross areas stained with hematoxylin and eosin, periodic acid-Schiff (PAS), Von Kossa’s phosphate stain, and Alizarin Red S showed multiple foci of calcium salts, some as fine granules within or coating degenerating, PAS-positive myocardial fibers and others as small cohesive plaques (Fig 2). Uncalci¢ed areas exhibited focal fibrosis, fiber hypertrophy, and a patchy but generalized myocardial fiber swelling with hyaline change. Iron stains of several calcific areas were negative. Histological examination of the cardiac valves, endocardium, and coronary arteries revealed no calcium deposits. The kidneys showed homogenous nephrosis. The lungs, liver, and spleen were acutely congested. The parathyroid glands were not enlarged, and the skeleton and bone marrow were normal. The brain was edematous with evidence of increased intracranial pressure. The remainder of the autopsy revealed no other ectopic areas of calcification. Duplicate portions of the fixed left ventricle averaged 38 mEq of total calcium per kilogram (fresh buffered formalin’s calcium: 1.6 mEq/liter). Three fresh, normal hearts removed from children during routine autopsy averaged 4.0 mEq of calcium per kilogram, slightly less than normal adult values.

Comment

Two categories traditionally comprise ectopic calcification: (1) the dystrophic, an accumulation of minerals in previously injured and often collagenized tissue unassociated with alterations in serum calcium and phosphate; and (2) the metastatic, a mineral accumulation on apparently intact tissues with a characteristic deposition pattern occurring against a background of increased available circulating calcium. Accounts of puzzling variations, for example, idiopathic arterial calcification of infancy or solitary lung calcification after calcium infusion continue to appear, however. Gore and Arons noted the association of azotemia and accelerated myocardial calcification, and Hamme and Ranstrom more recently cited the relatively large proportion of myocardial infarcts that are associated with calcification in children. Although the experimental work of Meroney et al suggests that traumatized skeletal muscle in the uremic dog may increase its calcium content over tenfold within 6 days, this finding has not been confirmed in cardiac muscle. Clowes and Simeone called attention to the drop of both ionized and total serum calcium during the immediate postoperative period of patients undergoing major surgery, but did not offer an opinion concerning the locus of deposition of this calcium. Lately, Selye and co-workers have described a series of rapidly developing changes with calcium deposition in a wide variety of tissues, including the myocardium. What pathogenic relationship, if any, these experimental “cardiopathies” may have to the case in question is not apparent.

The authors prefer to regard this case as an instance of accelerated dystrophic myocardial calcification: “accelerated” because of calcium deposits in a heart that grossly and histochemically lacked them 6 days previously; “dystrophic” because of localized deposition in damaged tissue coupled with a lack of clinical or chemical evidence to suggest elevated total serum calcium or phosphate. The pathogenesis of the changes in this child’s heart is not known. From what may be inferred from references cited above, a combination of myocardial damage, preceding and during surgery, azotemia, calcium salt infusions, and the patient’s youth may have been more important than any single factor. In an as yet incomplete pilot study, the authors have been able to induce changes in four uremic dogs’ myocardiums that closely resemble those reported here.

Summary

The myocardium of an eight-year-old boy apparently calcified within 6 days after open heart surgery for multiple congenital defects. It is thought that this probably represents an accelerated variant of dystrophic myocardial calcification.

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Generic and Trade Names of Drugs

Mannitol—Mannitol.

Isoproterenol hydrochloride—Isuprel Hydrochloride.

Hydrocortisone—Cortef, Cortifan, Cortril, Hycortole, Hydrocortone.

References